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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,677	09/14/2001	Christine Libon	PF95PCTSEQ/D	9128

25666 7590 12/23/2003

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EXAMINER	
FIELD, TAMMY K	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/936,677	LIBON ET AL.
	Examiner	Art Unit
	Tammy K. Field	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-61* is/are pending in the application.

4a) Of the above claim(s) *29-44,47-49,52-55,and 60-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,46,50,51 and 56-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *29-44,47-49,52-55,60 and 61* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Election/Restrictions

1. Responsive to Applicant's election of Group II, received October 31, 2003 with traverse on the grounds that the instant invention involved has a common special technical innovation is not found persuasive because the art of d'Hinterland, *et al.* (French Patent #2,596,064 published September 25, 1987) in the restriction requirement mailed from the Office September 24, 2003 determined the Unity of Invention is not fulfilled because there was not a technical feature that is "special", in that the technical feature does not define a contribution over the art (see restriction requirement mailed from the Office September 24, 2003). As such, a method for preparation of a membrane fraction of gram-negative bacteria comprising proteoglycans lacks Unity of Invention.

Applicant's further traversal that the Species are pharmacologically related is not found persuasive because the Species of the Invention of Group I identify different chemical and structural entities, *i.e.* cytokines, hormones, growth factors, cellular compounds, DNAs, RNAs, ribosome family, and heat shock protein family that necessitate different immunological responses. Furthermore, Species 1 of the Invention of Group II identify different modes of anticancer treatment, *i.e.* chemotherapy, radiotherapy, protease inhibitor, and compound with anti-angiogenic activity that necessitate different responses, and Species 2 of the Invention of Group II identify different cancers, *i.e.* bladder cancer, prostate cancer, colon cancer, liver cancer, and malignant melanomas that also necessitate different responses to treatment of Species I of the Invention of Group II.

The restriction requirement is still deemed proper and is therefore made **FINAL**.

2. Claims 29-44, 47-49, 52-55, and 60-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention and/or Species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in received in the Office October 31, 2003.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

In regard to applicant's claim for foreign priority based on the French application, 99 03154 03/15/1999 filed on May 8, 2000, it is noted that the Office has not received a certified copy of the translation of this application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 45-46, 50-51, 56-59 are rejected under 35 USC 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, *i.e.* "The use of Claim 29 for preparing pharmaceutical composition" and "combination product for use" (emphasis added) which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 45-46, 50-51, 56-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompass a method using membrane fractions comprising proteoglycans for preparing a pharmaceutical composition administered in combination with an anticancer treatment comprising chemotherapy for preventing and/or treating malignant melanomas. Further claims encompass using combination products simultaneously, separately, or at intervals.

The teachings of the specification are limited to the *in vitro* proliferation of PBMC in the presence of FMKp, the production of TNF-α and IL-12 p70 by blood monocytes, and production of the membrane fraction of *K. pneumoniae*. The specification further teaches that *in vitro* FMKp is an immunostimulant that induces the proliferation of PBMC from human blood that affects monocytes.

The specification fails to show how the membrane fraction of Gram-negative bacterium, comprising proteoglycans are used for preparing an anticancer pharmaceutical composition in combination with chemotherapy able to prevent and/or treat malignant melanomas, *e.g. in vitro* shrinking of tumors of malignant melanomas in a effective concentration of proteoglycans in

combination with any type of chemotherapeutic schedule in either an *in vitro* or an *in vivo* environmental condition.

Yen-Maguire, Y.P. *et al.* (US Patent No. 5,242,806 published September 7, 1993) teach various methods for conducting cytotoxicity assays on tumor cells such as *in vitro* chemosensitivity including human tumor cloning assay, fluorescent cytoprint assay, and a tritiated thymidine uptake assay that incorporates the radionucleotides during DNA synthesis as an indication of cell viability and proliferation wherein tumor preparations are exposed to drugs, either short-term or continuously and cultured in medium at column 2, line 43 – column 5, line 43. Yen-Maguire, Y.P. *et al.* further teach in a review of 2300 patients, the correlation between an in vitro chemosensitivity assay and actual patient response and that these types of studies begin to supply reliable data supporting the general use of an assay to predict patient response to chemotherapeutics at column 5, lines 44- column 6, line 20.

Burton, R.C. 2000. (CA Cancer J. Clin. 50(4):209-213) teaches because results with chemotherapy for melanoma have not improved in over a quarter of a century of randomized controlled trials, and further stresses the promise (emphasis added) of biological agents and vaccines at page 212, paragraph 2. Burton, R.C. further teaches that nevertheless, although there is good evidence that human melanoma is immunogenic and that the immune system can respond, biological therapies and vaccines have, as yet, no established place in the management of the disease.

In view of the state of the prior art set forth supra, it would require undue experimentation to practice the claimed invention. Since the office does not have the facilities for examining and comparing applicants' anticancer treatment methods with the methods

disclosed in the prior art, the burden is on the Applicant(s) to provide evidence of why the claimed method is enabled. At present examination, Applicant(s) have not presented sufficient evidence to practice the claimed invention.

6. Claims 45-46, 50-51, 56-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation of "intended to be administered" because it is unclear from the specification what applicant intends. Do Applicants submit the claimed pharmaceutical composition may potentially be administered? Does the claimed invention delineate a *method of using* the pharmaceutical composition in combination with an anticancer treatment **or** a *method of preparing* a pharmaceutical composition in combination with an anticancer treatment? As such, respectfully submitted, the instant claims are unclear of the exact nature of the invention.

Clarification is required in order to overcome this rejection.

Therefore, for purposes of examination, the claims will be interpreted to read on membrane fractions comprising proteoglycans used in a method of preparing a pharmaceutical composition for administration by either simultaneous, separate, or at intervals in combination with an anticancer treatment comprising chemotherapy for preventing and/or treating malignant melanomas.

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 45-46, 50-51, 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shyjan, A.W. (U.S. Patent 5,674,739 issued October 7, 1997).

The claims are drawn to membrane fractions comprising proteoglycans used in a method of preparing a pharmaceutical composition for administration by either simultaneous, separate, or at intervals in combination with an anticancer treatment comprising chemotherapy for preventing and/or treating malignant melanomas.

Shyjan, A.W. teach that during clinical trails, by monitoring the level of expression of romy030 (030 gene), a protocol for suitable chemotherapeutic anticancer drugs can be developed and monitored based on the metastatic potential of tumor cells at column 41, line 43- column, line 5. Shyjan, A.W. also teach that cell surface receptors such as proteoglycans facilitate tumor

attachment and are an important step in invasion and metastases at column 2, lines 48-51. Shyjan, A.W. further teach insight into the complex events that lead from normal cellular growth to neoplasia, invasion and metastasis is crucial for the development of effective diagnostic and therapeutic strategies and that therapeutic treatments such as differentially expressed genes and/or gene products, *e.g.* proteoglycans, could represent targets for therapeutic treatment of various forms of tumor progression of pre-neoplastic lesions to malignant tumors at column 3, lines 12- 36.

Shyjan, A.W. does not further teach the involvement of proteoglycans for preparing a pharmaceutical composition in a therapeutic treatment regiment.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the use of romy030 with a proteoglycan gene or gene product for preparing a pharmaceutical composition in combination with a chemotherapeutic anticancer treatment.

The person of ordinary skill in the art at the time the invention was made would utilize all available options for designing enhanced methods for preparing a pharmaceutical composition administered in combination with an anticancer treatment comprising chemotherapy for preventing and/or treating malignant melanomas.

Thus, Shyjan, A.W. render obvious the claimed invention.

Status of the Claims

8. No claims are allowed.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (703) 305-4447. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TKF

Tammy K. Field

December 15, 2003

TAMMY K. FIELD
PRIMARY EXAMINER
12/15/03